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* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1          Web Page for STN Seminar Schedule - N. America
 NEWS  2  DEC 01  ChemPort single article sales feature unavailable
 NEWS  3  JUN 01  CAS REGISTRY Source of Registration (SR) searching
                  enhanced on STN
 NEWS  4  JUN 26  NUTRACEUT and PHARMAML no longer updated
 NEWS  5  JUN 29  IMSCOPROFILE now reloaded monthly
 NEWS  6  JUN 29  EPFULL adds Simultaneous Left and Right Truncation
                  (SLART) to AB, MCLM, and TI fields
 NEWS  7  JUL 09  PATDPAFULL adds Simultaneous Left and Right
                  Truncation (SLART) to AB, CLM, MCLM, and TI fields
 NEWS  8  JUL 14  USGENE enhances coverage of patent sequence location
                  (PSL) data
 NEWS  9  JUL 27  CA/CAplus enhanced with new citing references
 NEWS 10  JUL 16  GBFULL adds patent backfile data to 1855
 NEWS 11  JUL 21  USGENE adds bibliographic and sequence information
 NEWS 12  JUL 28  EPFULL adds first-page images and applicant-cited
                  references
 NEWS 13  JUL 28  INPADOCDB and INPAFAMDB add Russian legal status data
 NEWS 14  AUG 08  Improve STN by completing a survey and be entered to
                  win a gift card
 NEWS 15  AUG 10  Time limit for inactive STN sessions doubles to 40
                  minutes
 NEWS 16  AUG 17  CAS REGISTRY, the Global Standard for Chemical
                  Research, Approaches 50 Millionth Registration
                  Milestone

 NEWS EXPRESS MAY 26 09 CURRENT WINDOWS VERSION IS V8.4,
              AND CURRENT DISCOVER FILE IS DATED 06 APRIL 2009.

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*                                                                       *
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* * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 11:16:37 ON 18 AUG 2009

=> file reg
COST IN U.S. DOLLARS                                 SINCE FILE      TOTAL
                                                        ENTRY     SESSION
FULL ESTIMATED COST                                      0.22        0.22
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DICTIONARY FILE UPDATES: 17 AUG 2009 HIGHEST RN 1174495-28-3

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=>
Uploading C:\Program Files\Stnexp\Queries\10539845-RCE-2.str

L1 STRUCTURE UPLOADED

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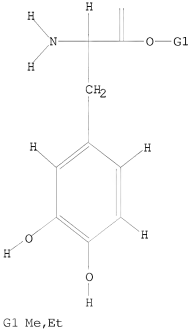
L1 HAS NO ANSWERS
L1 STR



G1 Me,Et

Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SEARCH INITIATED 11:17:17 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      355 TO ITERATE

100.0% PROCESSED      355 ITERATIONS                                 6 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:         5970 TO     8230
PROJECTED ANSWERS:               6 TO      266

L2            6 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 11:17:20 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -     6735 TO ITERATE

100.0% PROCESSED     6735 ITERATIONS                              100 ANSWERS
SEARCH TIME: 00.00.01

L3          100 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                              185.88     186.10

FILE 'CAPLUS' ENTERED AT 11:17:24 ON 18 AUG 2009
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FILE COVERS 1907 - 18 Aug 2009  VOL 151 ISS 8
FILE LAST UPDATED: 17 Aug 2009  (20090817/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED:  Jun 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE:  Jun 2009

CAplus now includes complete International Patent Classification (IPC)
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of databases have been updated to include new citing references
information.  This enhancement may impact record import into
database management software.  For additional information, refer
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to NEWS 9.

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=> s l3
L4          446 L3

=> s l4 not py > 2002
       8666946 PY > 2002
L5          311 L4 NOT PY > 2002

=> s l4 not py > 2001
       9621968 PY > 2001
L6          298 L4 NOT PY > 2001

=> s l6 and levodopa
          2934 LEVODOPA
L7          30 L6 AND LEVODOPA

=> s l6 and tyrosine transport
        182514 TYROSINE
        842295 TRANSPORT
           172 TYROSINE TRANSPORT
                (TYROSINE(W)TRANSPORT)
L8            0 L6 AND TYROSINE TRANSPORT

=> d l7 ibib abs hitstr 1-
YOU HAVE REQUESTED DATA FROM 30 ANSWERS - CONTINUE? Y/(N):y

L7   ANSWER 1 OF 30  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        1999:817387  CAPLUS
DOCUMENT NUMBER:         132:273598
TITLE:                   CHF-1301, Chiesi Farmaceutici SpA
AUTHOR(S):               De Ceballos, Maria
CORPORATE SOURCE:        Cajal Institute, Madrid, 28002, Spain
SOURCE:                  Current Opinion in Central & Peripheral Nervous System
                         Investigational Drugs (1999), 1(5), 649-653
                         CODEN: COCDFA; ISSN: 1464-844X
PUBLISHER:               Current Drugs Ltd.
DOCUMENT TYPE:           Journal; General Review
LANGUAGE:                English
AB   A review with 38 refs. CHF-1301 (levodopa Me ester; LDME) is a
     levodopa prodrug that has been developed by Chiesi for the
     treatment of Parkinson's disease (PD).  The product was launched as an
     injectable formulation in Italy in July 1999.  Chiesi is also developing
     CHF-1512, which is a combination of LDME and carbidopa.  This agent is
     potentially useful for the treatment of PD and is in phase III clin.
     trials for this indication.
IT   7101-51-1P, CHF 1301
     RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or
     effector, except adverse); BPR (Biological process); BSU (Biological
     study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC
     (Process); USES (Uses)
        (pharmacol. of CHF-1301 for treatment of Parkinson's disease)
RN   7101-51-1  CAPLUS
CN   L-Tyrosine, 3-hydroxy-, methyl ester  (CA INDEX NAME)

Absolute stereochemistry.  Rotation (+).
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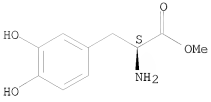


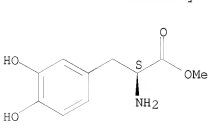
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1998:381119 CAPLUS
DOCUMENT NUMBER: 129:117723
ORIGINAL REFERENCE NO.: 129:23993a,23996a
TITLE: Circling behavior in 6-hydroxydopamine-lesioned rats given pulsed levodopa is reduced more by lesions in the entopeduncular nucleus/substantia nigra pars reticulata than in the subthalamic nucleus
AUTHOR(S): Honey, C. R.; Shen, H.
CORPORATE SOURCE: Division of Neurosurgery, University of British Columbia, Vancouver, BC, V6T 1Z3, Can.
SOURCE: Neuroscience Letters (1998), 249(2,3), 151-154
CODEN: NELED5; ISSN: 0304-3940
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Rats unilaterally lesioned with 6-hydroxydopamine to deplete brain striatal dopamine received daily injections of levodopa Me ester in combination with benserazide. Delayed lesions in the subthalamic nucleus (Group 2) or entopeduncular nucleus and substantia nigra pars reticulata (Group 3) were made, unilateral to the dopamine depletion. Apomorphine-induced rotation was reduced in Group 2 vs. sham-operated controls and in Group 3 vs. Group 2. Thus, the enhanced apomorphine-induced rotation behavior in this model is mediated through both the striatopallidal and striatonigral pathways.

IT 1421-65-4, Levodopa methyl ester hydrochloride
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(levodopa effects on circling behavior in 6-hydroxydopamine brain-lesioned rats are reduced more by lesions in entopeduncular nucleus/substantia nigra pars reticulata than in subthalamic nucleus)
RN 1421-65-4 CAPLUS
CN L-Tyrosine, 3-hydroxy-, methyl ester, hydrochloride (1:1) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

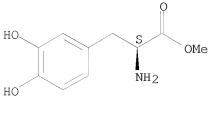


● HCl

OS.CITING REF COUNT: 9 THERE ARE 9 CAPLUS RECORDS THAT CITE THIS RECORD (9 CITINGS)
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1998:212852 CAPLUS
DOCUMENT NUMBER: 128:290145
ORIGINAL REFERENCE NO.: 128:57323a,57326a
TITLE: Effects of the nicotinic acetylcholine receptor agonist SIB-1508Y on object retrieval performance in MPTP-treated monkeys: comparison with levodopa treatment
AUTHOR(S): Schneider, J. S.; Van Velson, M.; Menzaghi, F.; Lloyd, G. K.
CORPORATE SOURCE: Department of Pathology, Anatomy and Cell Biology, Thomas Jefferson University, Philadelphia, PA, 19107, USA
SOURCE: Annals of Neurology (1998), 43(3), 311-317
CODEN: ANNED3; ISSN: 0364-5134
PUBLISHER: Lippincott-Raven Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study assessed the relative potencies of levodopa /benserazide and the nicotinic acetylcholine receptor agonist SIB-1508Y on reversal of cognitive and motor deficits in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-treated monkeys performing an object retrieval task. Monkeys previously taught to perform this task developed significant cognitive deficits after chronic low-dose MPTP exposure. These monkeys then received addnl. MPTP treatment to superimpose a parkinsonian movement disorder on their preexisting cognitive deficits. Levodopa/benserazide treatment significantly improved motor aspects of object retrieval performance but did not significantly improve cognition. SIB-1508Y (1 mg/kg) alone did not result in a statistically significant improvement in cognition or motor function in symptomatic MPTP-lesioned animals with deficits in both of these areas. However, the combination of SIB-1508Y and levodopa/benserazide caused significant improvements in both cognition and motor aspects of task performance, and did so at one third to one sixth of the levodopa dose necessary to improve only motor function. These results suggest the potential usefulness of SIB-1508Y and levodopa as adjunctive therapies to improve at least some of the cognitive and motor deficits associated with Parkinson's disease.
IT 7101-51-1, L-Dopa methyl ester
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of nicotinic acetylcholine receptor agonist SIB-1508Y and levodopa/benserazide on object retrieval performance in MPTP-treated monkeys in relation to Parkinson's disease treatment)
RN 7101-51-1 CAPLUS
CN L-Tyrosine, 3-hydroxy-, methyl ester (CA INDEX NAME)

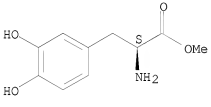
Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 35 THERE ARE 35 CAPLUS RECORDS THAT CITE THIS RECORD (35 CITINGS)
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1997:638945 CAPLUS
DOCUMENT NUMBER: 127:215147
ORIGINAL REFERENCE NO.: 127:41709a,41712a
TITLE: Effect of L-dopa alone and with benserazide on the spontaneous activity of striatal neurons in normal and 6-hydroxydopamine-lesioned rats. [Erratum to document cited in CA127:13335]
AUTHOR(S): Chang, W. Y.; Webster, R. A.
CORPORATE SOURCE: National Research Institute of Chinese Medicine, Taipei, 11221, Taiwan
SOURCE: British Journal of Pharmacology (1997), 122(2), 400
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Stockton
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In the abstract of the above paper the final sentence should read: 6. This study also shows the chronic levodopa/PDI treatment reduces the compensating increased activity of surviving dopaminergic neurons and the functional supersensitivity to dopamine and suggests that the long term administration of levodopa may reduce its own utilization and activity in the striatum and in the treatment of Parkinson's Disease.
IT 7101-51-1, L-Dopa methyl ester
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(L-dopa alone and with benserazide effect on spontaneous activity of striatal neurons in normal and hydroxydopamine-lesioned animals (Erratum))
RN 7101-51-1 CAPLUS
CN L-Tyrosine, 3-hydroxy-, methyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L7 ANSWER 5 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1997:318886 CAPLUS
DOCUMENT NUMBER: 127:13335
ORIGINAL REFERENCE NO.: 127:2594h,2595a
TITLE: Effect of L-dopa alone and with benserazide on the spontaneous activity of striatal neurons in normal and 6-hydroxydopamine-lesioned rats
AUTHOR(S): Chang, W. Y.; Webster, R. A.
CORPORATE SOURCE: National Research Institute of Chinese Medicine, Taipei, 11221, Taiwan
SOURCE: British Journal of Pharmacology (1997), 121(2), 331-337
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Stockton
DOCUMENT TYPE: Journal
LANGUAGE: English

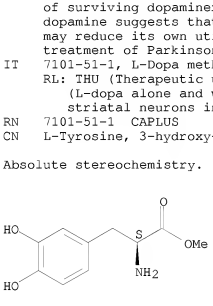
AB The effects of L-dopa Me ester (LDME), an analog of levodopa, on the spontaneous activity of dopamine sensitive neurons in the rat striatum, after 6-hydroxydopamine induced degeneration of the nigrostriatal tract were compared with those in unlesioned animals both in the absence and presence of benserazide, a peripheral DOPA decarboxylase inhibitor (PDI). Studies were performed at 5-7 days post lesion (group 1 animals), at 21 days (group 2) when denervation supersensitivity was evident by contralateral turning to apomorphine and at the same time but following 7 days dosing with LDME plus benserazide (group 3). In unlesioned animals, LDME alone inhibited spontaneous firing by some 45% over 60 min including a marked but transient early phase which was still present in all lesioned animals even though the later inhibition was significantly reduced in group 1 and 3 animals. When given after benserazide in unlesioned animals LDME still produced a similar level of overall inhibition but without the early phase. The lesion reduced the overall inhibition, except in group 2 animals, and after chronic dosing (group 3) it was almost absent. It is proposed that since the early inhibition with LDME alone is still seen after lesion of the nigrostriatal tract but not after the PDI benserazide, it is caused by peripherally formed dopamine and that as the delayed inhibition with LDME alone and after benserazide are all reduced by nigrostriatal lesions, as is its amphetamine like ipsilateral turning, that this depends on locally (striatal) synthesized dopamine. This study also shows that chronic levodopa/PDI treatment reduces the compensating increased activity of surviving dopaminergic neurons and the functional supersensitivity to dopamine suggests that the long term administration of levodopa may reduce its own utilization and activity in the striatum and in the treatment of Parkinson's Disease.

IT 7101-51-1, L-Dopa methyl ester
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(L-dopa alone and with benserazide effect on spontaneous activity of striatal neurons in normal and hydroxydopamine-lesioned animals)

RN 7101-51-1 CAPLUS

CN L-Tyrosine, 3-hydroxy-, methyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



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L7 ANSWER 6 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1997:185111 CAPLUS

DOCUMENT NUMBER: 126:242888

ORIGINAL REFERENCE NO.: 126:46901a,46904a

TITLE: L-DOPA ethyl ester to treat Parkinson's disease

INVENTOR(S): Milman, Isaac; Veinberg, Alexander; Atlas, Daphne; Melamed, Eldad

PATENT ASSIGNEE(S): Yissum Research Development Company of the Hebrew University of Jerusalem, Israel; Teva Pharmaceutical Industries Ltd.

SOURCE: U.S., 7 pp., Cont.-in-part of U.S. 5,525,631. CODEN: USXXAM

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5607969	A	19970304	US 1995-442888	19950517
US 5354885	A	19941011	US 1992-995847	19921224
EP 867179	A1	19980930	EP 1998-101741	19931224
EP 867179	B1	20000906		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
US 5525631	A	19960611	US 1994-276196	19940718
GR 3034867	T3	20010228	GR 2000-402556	20001116
PRIORITY APPLN. INFO.:			US 1992-995847	A1 19921224
			US 1994-276196	A2 19940718
			EP 1993-120894	A3 19931224

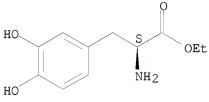
AB Patients suffering from Parkinson's disease are treated by administering a composition which contains an active ingredient and a pharmaceutically acceptable carrier. The active ingredient comprises L-DOPA Et ester in an amount which is at least 97% by weight of the active ingredient and L-DOPA in an amount which is less than 1% by weight of the active ingredient.

IT 37178-37-3, L-Tyrosine, 3-hydroxy-, ethyl ester
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(L-DOPA Et ester to treat Parkinson's disease)

RN 37178-37-3 CAPLUS

CN L-Tyrosine, 3-hydroxy-, ethyl ester (CA INDEX NAME)

Absolute stereochemistry.



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 7 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1996:258836 CAPLUS
DOCUMENT NUMBER: 125:1269
ORIGINAL REFERENCE NO.: 125:291a,294a
TITLE: Levodopa ethylester: A novel rescue therapy for response fluctuations in Parkinson's disease
AUTHOR(S): Djaldetti, Ruth; Melamed, Eldad
CORPORATE SOURCE: Department Neurology, Beilinson Medical Center, Petah Tiqva, 49100, Israel
SOURCE: Annals of Neurology (1996), 39(3), 400-4
CODEN: ANNED3; ISSN: 0364-5134
PUBLISHER: Little, Brown
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In Parkinson's disease (PD), response fluctuations may be due, in part, to pharmacokinetic problems including poor solubility of levodopa and difficulties in its absorption. We administered levodopa

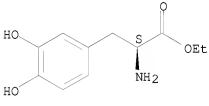
ethylester (LDEE), a new highly soluble prodrug of levodopa, by s.c. and i.m. injections to PD patients with response fluctuations, in an open trial to examine its safety and efficacy. Various doses of LDEE (150-400 mg) turned patients "on" with a high success rate (43 of 45 injections). Latencies to "turning on" decreased and duration of on responses increased in a dose-dependent manner. LDEE, given either s.c. or i.m., produced similar beneficial effects and induced rapid and sustained elevations in plasma levodopa levels. The drug was well tolerated with only minor and negligible side effects. Study suggests that s.c. and i.m. administration of LDEE may be advantageous as a novel therapeutic strategy for response fluctuations. It may be particularly useful to rapidly and predictably rescue patients from a variety of disabling "off" situations.

IT 37178-37-3, L-Tyrosine, 3-hydroxy-, ethyl ester
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(levodopa ethylester as a novel rescue therapy for response fluctuations in humans with Parkinson's disease)

RN 37178-37-3 CAPLUS

CN L-Tyrosine, 3-hydroxy-, ethyl ester (CA INDEX NAME)

Absolute stereochemistry.



OS.CITING REF COUNT: 13 THERE ARE 13 CAPLUS RECORDS THAT CITE THIS RECORD (13 CITINGS)

L7 ANSWER 8 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER:	1996:160059 CAPLUS
DOCUMENT NUMBER:	124:250716
ORIGINAL REFERENCE NO.:	124:46173a,46176a
TITLE:	Effect of subcutaneous administration of levodopa ethyl ester, a soluble prodrug of levodopa, on dopamine metabolism in rodent striatum: Implication for treatment of Parkinson's disease
AUTHOR(S):	Djaldetti, Ruth; Atlas, Daphne; Melamed, Eldad
CORPORATE SOURCE:	Department Neurology, Beilinson Medical Center, Petah Tiqva, 49100, Israel
SOURCE:	Clinical Neuropharmacology (1996), 19(1), 65-71 CODEN: CLNEDB; ISSN: 0362-5664
PUBLISHER:	Lippincott-Raven
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB Levodopa Et ester (LDEE), a highly soluble prodrug of levodopa, was synthesized and administered to mice and rats s.c. or i.p. Striatal levels of levodopa, dopamine, and the dopamine metabolite 3,4-dihydroxyphenylacetic acid (DOPAC) were determined using high-performance liquid chromatog. with electrochem. detection and compared with those obtained after i.p. injections of levodopa. LDEE injections produced significant and rapid elevations of striatal levodopa, dopamine, and DOPAC, which were similar to those achieved after levodopa administration, with similar dose-response curves. The elevations achieved by LDEE given s.c. were

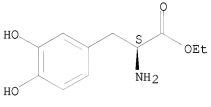
higher than those achieved after i.p. administration and lasted for longer periods. In addition, i.p. administration of levodopa or LDEE to rats with unilateral 6-hydroxydopamine (6-OHDA) nigral lesions produced similar contraversive circling responses. We suggest that LDEE may be a beneficial antiparkinsonian agent. It has potential pharmacokinetic advantages that are superior to those of levodopa itself, and its s.c. administration may become an effective rescue strategy to overcome "off" situations in patients with Parkinson's disease and response fluctuations.

IT 37178-37-3, L Dopa ethyl ester
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(s.c. administration of levodopa Et ester effect on dopamine metabolism in striatum in relation to Parkinson's disease treatment)

RN 37178-37-3 CAPLUS

CN L-Tyrosine, 3-hydroxy-, ethyl ester (CA INDEX NAME)

Absolute stereochemistry.



OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)

L7 ANSWER 9 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER:	1994:235986 CAPLUS
DOCUMENT NUMBER:	120:235986
ORIGINAL REFERENCE NO.:	120:41541a,41544a
TITLE:	The effects of chronic continuous versus intermittent levodopa treatments on striatal and extrastriatal D1 and D2 dopamine receptors and dopamine uptake sites in the 6-hydroxydopamine lesioned rat - an autoradiographic study
AUTHOR(S):	Gnanalingham, Kanna K.; Robertson, Robert G.
CORPORATE SOURCE:	Experimental Neurology and Myology Group, Department of Cell and Structural Biology, Stopford Building, University of Manchester, Oxford Road, M13 9PT, Manchester, UK
SOURCE:	Brain Research (1994), 640(1-2), 185-94 CODEN: BRREAP; ISSN: 0006-8993
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB The effects of chronic 'continuous' infusion and 'intermittent' modes of levodopa/carbidopa administration on apomorphine induced circling behavior, DA uptake sites (labeled with [3H]mazindol) and D1 and D2 DA receptor binding (labeled with [3H]SCH 23390 and [3H]sulpiride, resp.) were investigated in rats with unilateral 6-OHDA lesions of the medial forebrain bundle. The circling behavior in response to apomorphine was greatly enhanced following chronic 'intermittent' but not 'continuous' levodopa treatments. Following the 'intermittent' regime, the lower dose of apomorphine induced a period of intense circling with delayed onset and rapid offset, than in rats given either 'continuous' infusion of levodopa or saline. The 6-OHDA lesion itself induced gross depletion of [3H]mazindol binding in all striatal subregions, nucleus accumbens (NAc) and OT, but not frontal cortex. [3H]Sulpiride binding in the ventrolateral striatal quadrant was increased on the denervated side and this correlated with the peak contralateral

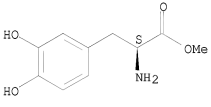
turns in response to 0.5 mg/kg apomorphine challenge. This asymmetry in striatal [3H]sulpiride binding was reduced in both groups of rats receiving levodopa. [3H]sulpiride binding in the NAc and OT and [3H]SCH 23390 binding in the striatum, NAc, OT and substantia nigra (SNr) were unaffected by DA denervation or either regime of levodopa treatments. 'Continuous' infusion and not 'intermittent' injections of levodopa reduced [3H]mazindol binding in the striatal subregions and the frontal cortex on both the denervated and intact sides. The potentiation of the behavioral response to apomorphine by chronic 'intermittent' levodopa treatment does not correspond with the levodopa induced alterations in striatal or extrastriatal DA receptors. In the same group of animals, the narrowing of the duration of response to the lower dose of apomorphine may mimic the fluctuations in response to levodopa, seen clin. in long-term levodopa treated parkinsonian patients.

IT 7101-51-1, Levodopa methyl ester
RL: BIOL (Biological study)
(dopaminergic systems in striatal and extrastriatal regions of brain response to continuous vs intermittent treatment with, median forebrain lesion effect on, parkinsonism treatment in relation to)

RN 7101-51-1 CAPLUS

CN L-Tyrosine, 3-hydroxy-, methyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 14 THERE ARE 14 CAPLUS RECORDS THAT CITE THIS RECORD (14 CITINGS)

L7 ANSWER 10 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1994:235267 CAPLUS

DOCUMENT NUMBER: 120:235267

ORIGINAL REFERENCE NO.: 120:41373a,41376a

TITLE: Simultaneous determination of levodopa methyl ester, levodopa, 3-O-methyldopa and dopamine in plasma by high-performance liquid chromatography with electrochemical detection

AUTHOR(S): Rondelli, Ivano; Acerbi, Daniela; Mariotti, Fabrizia; Ventura, Paolo

CORPORATE SOURCE: Chiesi Farm. S.p.A., Parma, 43100, Italy

SOURCE: Journal of Chromatography, B: Biomedical Sciences and Applications (1994), 653(1), 17-23
CODEN: JCBBEP; ISSN: 1387-2273

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A new procedure is described for the simultaneous determination of levodopa Me ester (LDME) and its biotransformation products levodopa (L-DOPA), 3-O-methyldopa (3-OMD) and dopamine (DA) in stabilized plasma samples, using reversed-phase high-performance liquid chromatog. A coulometric detector equipped with a dual-electrode system operating in the redox mode was used to simultaneously quantitate all compds. This system generated a double signal monitored by a dual-channel acquisition data system and allowed quantitation of compds. at the nanogram level. The intra- and inter-assay precision varied in the 2.4-6.9% and 3.2-9.1% ranges resp., whereas the recoveries were close to

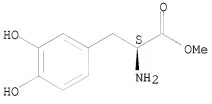
85% for L-DOPA and 3-OMD and 70% for DA and LDME. Samples may be stored at −80° for 15 days before anal. The method was applied to plasma samples after oral administration of LDME to rats, but it may also be suitable for human pharmacokinetic studies.

IT 7101-51-1, Levodopa methyl ester
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in blood plasma of humans by HPLC with electrochem. detection)

RN 7101-51-1 CAPLUS

CN L-Tyrosine, 3-hydroxy-, methyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 23 THERE ARE 23 CAPLUS RECORDS THAT CITE THIS RECORD (23 CITINGS)

L7 ANSWER 11 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1992:15515 CAPLUS

DOCUMENT NUMBER: 116:15515

ORIGINAL REFERENCE NO.: 116:2636h,2637a

TITLE: Effect of L-Dopa methylester and glutathione depletion on murine B16BL6 melanoma growth in vitro

AUTHOR(S): Thrall, Brian D.; Meadows, Gary G.

CORPORATE SOURCE: Coll. Pharm., Washington State Univ., Pullman, WA, 99164-6510, USA

SOURCE: Journal of Investigative Dermatology (1991), 97(6), 1073-7
CODEN: JIDEAE; ISSN: 0022-202X

DOCUMENT TYPE: Journal

LANGUAGE: English

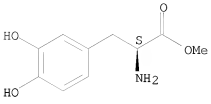
AB The cytotoxic and growth-inhibitory effect of levodopa methylester (LDME) in murine B16BL6 (BL6) melanoma cells after glutathione (GSH) depletion was studied in vitro. Pretreatment of BL6 cells with 50 μM buthionine sulfoximine (BSO) depleted GSH content by nearly 90% and enhanced the growth-inhibitory effect of even a minimally cytotoxic concentration of LDME. Radiothymidine incorporation into BL6 cells increased compared to untreated controls during the first 4 h of exposure to 0.2 mM LDME. However, pretreatment with BSO prevented this LDME-induced increase in radiothymidine incorporation. Because the percentage of cells in S-phase of the cell cycle was not altered, these results suggest that BSO exposure may be inhibiting unscheduled DNA synthesis, which could contribute to the cytotoxic effects of LDME. In addition, spectrophotometric studies indicated that in a cell-free system, GSH scavenged dopaquinone produced by the tyrosinase-mediated oxidation of LDME, presumably by formation of glutathionyldopa. Thus, enhancement of LDME cytotoxicity by BSO may also involve depleting the amount of GSH available for the nucleophilic addition to the quinone.

IT 7101-51-1, Levodopa methylester
RL: PRP (Properties)
(cytotoxicity and growth-inhibitory effects of, in mouse melanoma, glutathione role in)

RN 7101-51-1 CAPLUS

CN L-Tyrosine, 3-hydroxy-, methyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



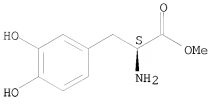
OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)

L7 ANSWER 12 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1991:464530 CAPLUS
DOCUMENT NUMBER: 115:64530
ORIGINAL REFERENCE NO.: 115:10939a,10942a
TITLE: Effect of acute levodopa on brain catecholamines after selective MAO and COMT inhibition in male rats
AUTHOR(S): Mannisto, P. T.; Tuomainen, P.; Toivonen, M.; Tornwall, M.; Kaakkola, S.
CORPORATE SOURCE: Dep. Pharmacol. Toxicol., Univ. Helsinki, Helsinki, SF-00170, Finland
SOURCE: Journal of Neural Transmission: Parkinson's Disease and Dementia Section (1990), 2(1), 31-43
CODEN: JNPSEJ; ISSN: 0936-3076
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Interactions between a selective catechol-O-methyltransferase (COMT) inhibitor OR-462 and a monoamine oxidase (MAO)-A inhibitor clorgyline were studied measuring concns. of L-dopa, dopamine and their metabolites in the rat hypothalamus and striatum after administration of levodopa /carbidopa (15/30 mg/kg i.p.). Part of the expts. were performed in rats pretreated with 6-OH-dopamine (6-OHDA) intracerebroventricularly (i.c.v.) to determine whether changes in dopamine metabolism occurred inside or outside catecholaminergic neurons. OR-462 was an effective COMT inhibitor at the doses 3 and 30 mg/kg i.p. Inhibition of 3-O-methyldopa (3-OMD) formation from L-dopa was reflected in the hypothalamus (45-81% decrease) and striatum (87-88% decrease), since 3-OMD penetrates the blood-brain barrier. Homovanillic acid (HVA) was decreased only in the striatum at 30 mg/kg of OR-462. Clorgyline (8 and 32 mg/kg i.p.) decreased 3,4-dihydroxyphenylacetic acid (DOPAC) formation in the hypothalamus and striatum by 61-91%. When given together, OR-462 and clorgyline elevated hypothalamic dopamine levels 3.2-4.6-fold, but striatal dopamine only 1.3-1.9-fold. The formation of 3-OMD and DOPAC remained suppressed and even brain HVA levels were decreased by 51-97%. 6-OHDA treatment decreased striatal and hypothalamic dopamine by 50% and noradrenaline by 75%. In these animals, levodopa/carbidopa increased brain L-dopa 2.4-4-fold, those of 3-OMD 1.2-1.7-fold compared to intact animals, but the synthesis and metabolism of dopamine and the effects of COMT and MAO inhibitors were not significantly changed. Levodopa/carbidopa treatment decreased significantly prolactin and TSH levels in serum, but none of the addnl. treatments changed this action.

IT 7101-51-1, Levodopa methylester
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(metabolism of, to catecholamines by brain, catechol methyltransferase and monoamine oxidase inhibition effect on)
RN 7101-51-1 CAPLUS
CN L-Tyrosine, 3-hydroxy-, methyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)

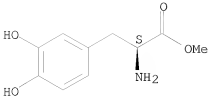
L7 ANSWER 13 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1991:240432 CAPLUS
DOCUMENT NUMBER: 114:240432
ORIGINAL REFERENCE NO.: 114:40385a,40388a
TITLE: Striatal D1 dopamine receptor morphochemistry following continuous or intermittent L-DOPA replacement therapy
AUTHOR(S): Ariano, Marjorie A.; Engber, Thomas M.; Susel, Zvi; Chase, Thomas N.
CORPORATE SOURCE: Coll. Med., Univ. Vermont, Burlington, VT, 05405, USA
SOURCE: Experimental Neurology (1991), 112(1), 112-18
CODEN: EXNEAC; ISSN: 0014-4886
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Striatal dopamine deafferentation has previously been found to diminish D1 dopamine receptor clustering in association with striatal cAMP-immunoreactive neurons. The administration of the dopamine precursor levodopa (L-DOPA) to animals with unilaterally placed 6-hydroxydopamine nigrostriatal tract lesions now appears to partially restore D1 dopamine receptor morphochem. organization in the deafferented striatum. Differences in the mode of levodopa delivery produced dissimilar D1 recovery patterns. The prodrug, L-DOPA Me ester, was administered in combination with the peripheral aromatic amino acid decarboxylase inhibitor, benserazide, to achieve consistent plasma levels of the dopamine precursor. Continuous levodopa infusion (100 mg/kg/day, i.p.) led to a slight dorsomedial reassocn. of D1 receptor binding sites with the post-synaptic cAMP transduction system on the deafferented side. In contrast, intermittent levodopa therapy (50 mg/kg, i.p., twice a day) produced a noticeable down regulation of the dopamine receptor system and also contributed to some region-specific recovery of the morphochem. pattern of D1 receptor binding site reaggregation with the postsynaptic cAMP second messenger transduction system. These results suggest that exogenous levodopa replacement therapy desensitizes striatal D1 dopamine receptors. This was substantiated using image anal. of densitometric histograms. The down regulation of D1 receptors is dependent on the levodopa treatment regimen employed. These findings provide a potential morphol. basis for the behavioral desensitization shown previously in response to chronic, intermittent levodopa administration.

IT 7101-51-1, Levodopa methyl ester
RL: BIOL (Biological study)
(levodopa effect on D1 receptor recovery in striatum after administration of)

RN 7101-51-1 CAPLUS
CN L-Tyrosine, 3-hydroxy-, methyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



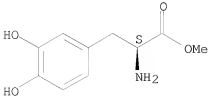
OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

L7 ANSWER 14 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1990:545247 CAPLUS
DOCUMENT NUMBER: 113:145247
ORIGINAL REFERENCE NO.: 113:24473a,24476a
TITLE: Responses of substantia nigra pars reticulata neurons to GABA and SKF 38393 in 6-hydroxydopamine-lesioned rats are differentially affected by continuous and intermittent levodopa administration
AUTHOR(S): Weick, Barton G.; Engber, Thomas M.; Susel, Zvi; Chase, Thomas N.; Walters, Judith R.
CORPORATE SOURCE: Exp. Therm. Branch, Natl. Inst. Neurol. Disord. Stroke, Bethesda, MD, 20892, USA
SOURCE: Brain Research (1990), 523(1), 16-22
CODEN: BRREAP; ISSN: 0006-8993
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Systemic administration of the selective D1 agonist SKF 38393 to rats with unilateral 6-hydroxydopamine-induced lesion of the brain nigrostriatal dopamine pathway induces contralateral turning and reduces firing rates of substantia nigra pars reticulata neurons. Chronically administered levodopa diminishes the contralateral turning induced by SKF 38393 in these animals. Twice daily injections (45-50 mg/kg, i.p.) of levodopa for 19 days also diminished the effects of SKF 38393 on substantia nigra pars reticulata activity. Concomitant with this change, chronic levodopa injections reversed the lesion-induced supersensitivity of substantia nigra pars reticulata neurons to iontophoresed GABA. Neither of these effects were produced by the continuous infusion of levodopa (90-100 mg/kg/day, i.p. by osmotic pump) for 19 days, a treatment that produces average daily blood levodopa levels similar to those produced by chronic levodopa injection. Large variations in circulating levodopa levels in 6-hydroxydopamine-lesioned rats may desensitize the behavioral responses to D1 dopamine agonist administration by down-regulating D1 and GABA receptor-mediated mechanisms of basal ganglia output through the substantia nigra pars reticulata.

IT 7101-51-1, Levodopa methyl ester
RL: BIOL (Biological study)
(behavior response to GABA and SKF-38393 and, after brain nigrostriatal lesions from hydroxydopamine)
RN 7101-51-1 CAPLUS
CN L-Tyrosine, 3-hydroxy-, methyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 13 THERE ARE 13 CAPLUS RECORDS THAT CITE THIS RECORD (13 CITINGS)

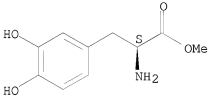
L7 ANSWER 15 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1989:484015 CAPLUS
DOCUMENT NUMBER: 111:84015
ORIGINAL REFERENCE NO.: 111:14041a,14044a
TITLE: Short-chain alkyl esters of L-dopa as prodrugs for rectal absorption
AUTHOR(S): Fix, Joseph A.; Alexander, Jose; Cortese, Margot; Engle, Karen; Leppert, Paula; Repta, Arnold J.
CORPORATE SOURCE: INTERx Res. Corp., Lawrence, KS, 66046, USA
SOURCE: Pharmaceutical Research (1989), 6(6), 501-5
CODEN: PHREEB; ISSN: 0724-8741
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The bioavailability of L-dopa following rectal administration of a series of short-chain alkyl esters of L-dopa was determined in rats and dogs. The esters were stable (>360 min) to hydrolysis in physiol. buffer. In vitro enzymic hydrolysis of the esters in plasma was species dependent, with the hydrolytic rate being faster in rat plasma (t1/2 < 5 min) than dog plasma (t1/2 = 68-181 min) or human plasma (t1/2 = 96-238 min). In vivo hydrolysis in dogs, as indicated by the L-dopa plasma profile following i.v. administration of the esters, was very rapid (high extravascular esterase activity). Significant L-dopa bioavailability was observed in rats following rectal administration of the Me (46%), Et (14%), iso-Pr (48%), Bu (100%), and 4-hydroxybutyl (13%) esters of L-dopa (rectal L-dopa absorption, <5%). In dogs, significant L-dopa bioavailability was also observed for the Me (28%), iso-Pr (30%), Bu (32%), and 4-hydroxybutyl (34%) esters of L-dopa in the presence of carbidopa. These highly water-soluble (>600 mg/mL) esters of L-dopa are potential candidates for controlled-release rectal delivery systems designed to provide more constant plasma L-dopa levels.

IT 7101-51-1P, L-Dopa methyl ester 37178-37-3P, L-Dopa ethyl ester
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as prodrug for controlled rectal delivery)

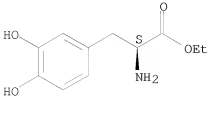
RN 7101-51-1 CAPLUS
CN L-Tyrosine, 3-hydroxy-, methyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 37178-37-3 CAPLUS
CN L-Tyrosine, 3-hydroxy-, ethyl ester (CA INDEX NAME)

Absolute stereochemistry.



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

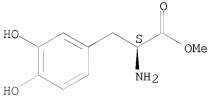
L7 ANSWER 16 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1989:433591 CAPLUS
DOCUMENT NUMBER: 111:33591
ORIGINAL REFERENCE NO.: 111:5625a,5628a
TITLE: Continuous and intermittent levodopa differentially affect basal ganglia function
AUTHOR(S): Juncos, Jorge L.; Engber, Thomas M.; Raisman, Rita; Susel, Zvi; Taibaut, Florence; Ploska, Alain; Agid, Yves; Chase, Thomas N.
CORPORATE SOURCE: Sch. Med., Emory Univ., Atlanta, GA, 30322, USA
SOURCE: Annals of Neurology (1989), 25(5), 473-8
CODEN: ANNED3; ISSN: 0364-5134
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of continuous and intermittent levodopa treatment on behavioral and biochem. indexes of basal ganglia function were compared in rats with unilateral 6-hydroxydopamine lesions of the nigrostriatal dopamine pathway. Animals treated for 30 days with intermittent levodopa exhibited behavioral sensitization manifested by an enhanced rotational response to apomorphine; the rotational response of rats treated with an equivalent dose of levodopa by continuous infusion did not differ from that of saline-treated controls. Dopamine receptor up-regulation in the denervated striatum relative to the intact striatum was statistically significant for D1 but not D2 receptors: This asymmetry in dopamine receptor levels was diminished following intermittent levodopa treatment. Glutamic acid decarboxylase activity, modestly elevated in all groups in the denervated striatum relative to the intact striatum, increased substantially over control values bilaterally as a result of intermittent, but not continuous, levodopa treatment. These findings suggest a relation between the schedule of chronic levodopa administration and the development of behavioral sensitization, possible as a consequence of alterations in neuronal systems located downstream from striatal dopamine receptors. The behavioral sensitization induced by chronic, intermittent dopaminomimetic treatment may serve as a model for motor fluctuations in Parkinson's disease.

IT 7101-51-1, Levodopa methyl ester
RL: BIOL (Biological study)
(brain basal ganglion function response to, mode of administration and behavioral sensitization in relation to)

RN 7101-51-1 CAPLUS
CN L-Tyrosine, 3-hydroxy-, methyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 54 THERE ARE 54 CAPLUS RECORDS THAT CITE THIS RECORD (54 CITINGS)

L7 ANSWER 17 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1988:411748 CAPLUS
DOCUMENT NUMBER: 109:11748

ORIGINAL REFERENCE NO.: 109:2005a,2008a
TITLE: Pharmaceutical compositions containing levodopa methyl ester for treatment of Parkinson's disease
INVENTOR(S): Chiesi, Paolo
PATENT ASSIGNEE(S): Chiesi Farmaceutici S.p.A., Italy
SOURCE: Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 252290	A2	19880113	EP 1987-107979	19870602
EP 252290	A3	19900124		
EP 252290	B1	19920603		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 76747	T	19920615	AT 1987-107979	19870602
ES 2042520	T3	19931216	ES 1987-107979	19870602
AU 8774053	A	19871217	AU 1987-74053	19870608
AU 605154	B2	19910110		
HU 43952	A2	19880128	HU 1987-2628	19870609
JP 63027428	A	19880205	JP 1987-143959	19870609
JP 2572768	B2	19970116		
ZA 8704128	A	19880224	ZA 1987-4128	19870609
CA 1303509	C	19920616	CA 1987-539220	19870609
US 4826875	A	19890502	US 1987-123118	19871120
US 5017607	A	19910521	US 1989-374273	19890630

PRIORITY APPLN. INFO.:
IT 1986-20737 A 19860610
IT 1987-19221 A 19870130
US 1987-56372 A3 19870601
EP 1987-107979 A 19870602

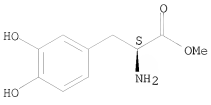
AB A composition comprising levodopa Me ester (I) and a carrier or diluent is used in the treatment of Parkinson's disease and correlated neurol. syndromes. A solution contained I 250, Me p-hydroxybenzoate 1.35, Pr p-hydrobenzoate 0.15, saccharin Na 10, citric acid·H2O 20, tri-Na citrate·2H2O 31.5 mg, orange flavor 0.002 mL, and water to 1 mL. The above solution was orally administered to patients with Parkinson's disease and plasma levels of I were measured; the absorption of I was very rapid and maximum concentration peak was reached at 40-45 min from the administration. Idiopathic parkinsonism patients were also treated by sublingual administration of 200 mg I in combination with oral administration of 25 mg carbidopa.

IT 1421-65-4, Levodopa methyl ester hydrochloride
114846-33-2 114846-34-3 114846-35-4
114846-36-5 114846-54-7 114924-77-5
114924-78-6 114924-79-7
RL: BIOL (Biological study)
(pharmaceutical, for treatment of Parkinson's disease)

RN 1421-65-4 CAPLUS

CN L-Tyrosine, 3-hydroxy-, methyl ester, hydrochloride (1:1) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



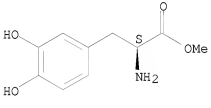
● HCl

RN 114846-33-2 CAPLUS
CN L-Tyrosine, 3-hydroxy-, methyl ester, mixt. with serine 2-[(2,3,4-trihydroxyphenyl)methyl]hydrazide (CA INDEX NAME)

CM 1

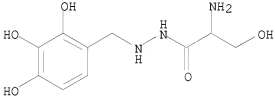
CRN 7101-51-1
CMF C10 H13 N O4

Absolute stereochemistry. Rotation (+).



CM 2

CRN 322-35-0
CMF C10 H15 N3 O5

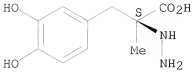


RN 114846-34-3 CAPLUS
CN L-Tyrosine, 3-hydroxy-, methyl ester, mixt. with (αS)-α-hydrazinyl-3,4-dihydroxy-α-methylbenzenepropanoic acid (CA INDEX NAME)

CM 1

CRN 28860-95-9
CMF C10 H14 N2 O4

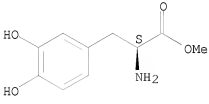
Absolute stereochemistry. Rotation (-).



CM 2

CRN 7101-51-1
CMF C10 H13 N O4

Absolute stereochemistry. Rotation (+).

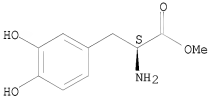


RN 114846-35-4 CAPLUS
CN L-Tyrosine, 3-hydroxy-, methyl ester, mixt. with N,α-dimethyl-N-2-propynylbenzeneethanamine (9CI) (CA INDEX NAME)

CM 1

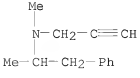
CRN 7101-51-1
CMF C10 H13 N O4

Absolute stereochemistry. Rotation (+).



CM 2

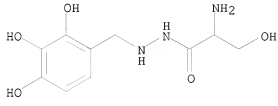
CRN 2323-36-6
CMF C13 H17 N



RN 114846-36-5 CAPLUS
CN L-Tyrosine, 3-hydroxy-, methyl ester, hydrochloride, mixt. with serine 2-[(2,3,4-trihydroxyphenyl)methyl]hydrazide, monohydrochloride (9CI) (CA INDEX NAME)

CM 1

CRN 14919-77-8
CMF C10 H15 N3 O5 . Cl H

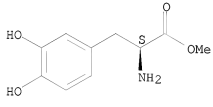


● HCl

CM 2

CRN 1421-65-4
CMF C10 H13 N O4 . Cl H

Absolute stereochemistry. Rotation (+).



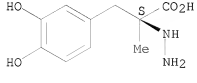
● HCl

RN 114846-54-7 CAPLUS
CN L-Tyrosine, 3-hydroxy-, methyl ester, hydrochloride, mixt. with (S)-α-hydrazino-3,4-dihydroxy-α-methylbenzenepropanoic acid monohydrochloride (9CI) (CA INDEX NAME)

CM 1

CRN 65132-60-7
CMF C10 H14 N2 O4 . Cl H

Absolute stereochemistry. Rotation (-).

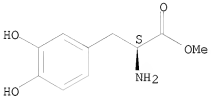


● HCl

CM 2

CRN 1421-65-4
CMF C10 H13 N O4 . Cl H

Absolute stereochemistry. Rotation (+).



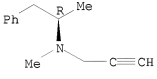
● HCl

RN 114924-77-5 CAPLUS
CN L-Tyrosine, 3-hydroxy-, methyl ester, hydrochloride, mixt. with (R)-N,α-dimethyl-N-2-propynylbenzeneethanamine hydrochloride (9CI) (CA INDEX NAME)

CM 1

CRN 14611-52-0
CMF C13 H17 N . Cl H

Absolute stereochemistry. Rotation (-).

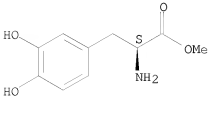


● HCl

CM 2

CRN 1421-65-4
CMF C10 H13 N O4 . Cl H

Absolute stereochemistry. Rotation (+).

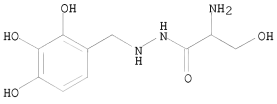


● HCl

RN 114924-78-6 CAPLUS
CN L-Tyrosine, 3-hydroxy-, methyl ester, mixt. with
(αR)-N,α-dimethyl-N-2-propynylbenzeneethanamine hydrochloride
and serine 2-[(2,3,4-trihydroxyphenyl)methyl]hydrazide, monohydrochloride
(9CI) (CA INDEX NAME)

CM 1

CRN 14919-77-8
CMF C10 H15 N3 O5 . Cl H

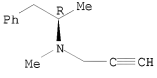


● HCl

CM 2

CRN 14611-52-0
CMF C13 H17 N . Cl H

Absolute stereochemistry. Rotation (-).

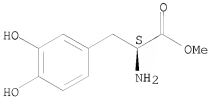


● HCl

CM 3

CRN 7101-51-1
CMF C10 H13 N O4

Absolute stereochemistry. Rotation (+).



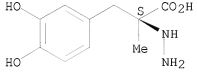
RN 114924-79-7 CAPLUS
CN L-Tyrosine, 3-hydroxy-, methyl ester, hydrochloride, mixt. with

(R)-N,α-dimethyl-N-2-propynylbenzeneethanamine hydrochloride and (S)-α-hydrazino-3,4-dihydroxy-α-methylbenzenepropanoic acid monohydrochloride (9CI) (CA INDEX NAME)

CM 1

CRN 65132-60-7
CMF C10 H14 N2 O4 . Cl H

Absolute stereochemistry. Rotation (-).

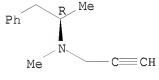


● HCl

CM 2

CRN 14611-52-0
CMF C13 H17 N . Cl H

Absolute stereochemistry. Rotation (-).

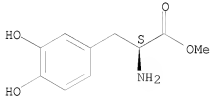


● HCl

CM 3

CRN 1421-65-4
CMF C10 H13 N O4 . Cl H

Absolute stereochemistry. Rotation (+).

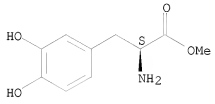


● HCl

IT 7101-51-1, Levodopa methyl ester

RL: BIOL (Biological study)
(pharmaceuticals, for treatment of Parkinson's disease)
RN 7101-51-1 CAPLUS
CN L-Tyrosine, 3-hydroxy-, methyl ester (CA INDEX NAME)

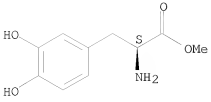
Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (9 CITINGS)

L7 ANSWER 18 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1986:417971 CAPLUS
DOCUMENT NUMBER: 105:17971
ORIGINAL REFERENCE NO.: 105:2861a,2864a
TITLE: Interaction between specific dietary factors and experimental chemotherapy of metastatic melanoma
AUTHOR(S): Meadows, Gary G.; Abdallah, Rokia M.; Starkey, Jean R.
CORPORATE SOURCE: Coll. Pharm., Washington State Univ., Pullman, WA, 99164-6510, USA
SOURCE: Cancer Chemotherapy and Pharmacology (1986), 16(3), 229-36
CODEN: CCPHDZ; ISSN: 0344-5704
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The single and combined effects of (a) dietary restriction of L-phenylalanine [63-91-2] and L-tyrosine [60-18-4], (b) levodopa Me ester [7101-51-1] chemotherapy, and (c) megadose ascorbate [50-81-7] supplementation on exptl. metastasis was determined in B16-BL6 melanoma in mice. Dietary restriction and levodopa methyl ester therapy inhibited tumor outgrowth, whereas ascorbate alone was inactive. In combination, however, the effect of dietary restriction and levodopa methyl ester chemotherapy was augmented by ascorbate. Tumor cells surviving this combination therapy (treated population) were isolated from the lungs of treated mice, and proved to be tumorigenic when inoculated s.c. into the back of naive mice. The resulting tumors grew more slowly than those produced by inoculation of similarly isolated control cells (control population), irresp. of whether the diet was adequate or deficient in phenylalanine and tyrosine. Failure of the treated tumor cell population to exhibit reduced sensitivity to the combination chemotherapy or, unlike the control population, to exhibit variation in pigmentation levels, suggests that the restriction of phenylalanine and tyrosine during drug therapy alters the tumor response to reduce heterogeneity and perhaps interferes with the emergence of drug resistance.
IT 7101-51-1
RL: BIOL (Biological study)
(metastatic melanoma treatment with ascorbate and, dietary factors effect on)
RN 7101-51-1 CAPLUS
CN L-Tyrosine, 3-hydroxy-, methyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 9 THERE ARE 9 CAPLUS RECORDS THAT CITE THIS RECORD (9 CITINGS)

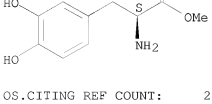
L7 ANSWER 19 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1986:81652 CAPLUS
DOCUMENT NUMBER: 104:81652
ORIGINAL REFERENCE NO.: 104:12793a,12796a
TITLE: Sequential inhibitory effects of antitumor agents related to levodopa and dopamine upon DNA synthetic enzymes
AUTHOR(S): Fitzgerald, George B.; Wick, Michael M.
CORPORATE SOURCE: Dep. Dermatol., Harvard Med. Sch., Boston, MA, 02115, USA
SOURCE: Biochemical Pharmacology (1986), 35(2), 271-5
CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Novel antitumor agents related to levodopa and dopamine exhibit a selective and rapid inhibition of DNA synthesis as measured by thymidine incorporation; the biochem. basis of the selective inhibition of tumor cells was examined The dihydroxybenzene derivs. were inhibited thymidylate synthase [9031-61-2] in situ at concns. ranging between 100 and 800 μM. The quinols did not inhibit partially purified thymidylate synthase, although the oxidized quinones did inhibit the enzyme at concns. between 10 and 100 μM. The inhibition of thymidylate synthase in situ by the dihydroxybenzene derivs. occurred after the inhibition of thymidine incorporation, indicating that an earlier event was critical to the inhibition of DNA synthesis. With the use of a novel in situ assay which measured the release of [3H]water from [5-3H]uridine in intact cells, it is shown that one of the earliest biochem. events is the inhibition of ribonucleotide reductase [9040-57-7] and that the inhibition of thymidylate synthase, which is delayed by approx. 30 min, was indirectly mediated possibly through effects on ribonucleotide reductase.

IT 7101-51-1
RL: BIOL (Biological study)
(DNA formation inhibition by, mechanism of, thymidylate synthase and ribonucleotide reductase in relation to)

RN 7101-51-1 CAPLUS
CN L-Tyrosine, 3-hydroxy-, methyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



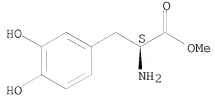
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L7 ANSWER 20 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1986:81641 CAPLUS
DOCUMENT NUMBER: 104:81641
ORIGINAL REFERENCE NO.: 104:12793a,12796a
TITLE: Influence of supplemental ascorbate on the antitumor activity of 5-hydroxydopa, a purported cytotoxic metabolite
AUTHOR(S): Pierson, Herbert F.; Meadows, Gary G.
CORPORATE SOURCE: Lab. Pharmacol. Exp. Ther., Natl. Cancer Inst., Bethesda, MD, 20205, USA
SOURCE: Cancer Letters (Shannon, Ireland) (1985), 29(2), 157-68
CODEN: CALEDQ; ISSN: 0304-3835
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 5-Hydroxydopa [16032-83-0], a known cytotoxic agent and the major metabolite formed from levodopa in the presence of ascorbate and mushroom tyrosinase in vitro, was assessed for its antitumor activity against i.p. and s.c. inoculated B16 melanoma, P388 leukemia, and L1210 leukemia in mice with and without supplemental ascorbate [50-81-7]. Treatment with 5-hydroxydopa failed to significantly increase survival of mice bearing i.p. or s.c. pigmented and nonpigmented B16 melanomas even though it inhibited local tumor growth. Treatment increased survival of both P388 and L1210 leukemias, and this increase was more pronounced in mice bearing i.p. tumors than in mice bearing s.c. tumors. This treatment significantly decreased final tumor weight of both leukemias implanted s.c., and inhibited ascites formation in mice inoculated with i.p. tumors. Ascorbate supplementation decreased or abrogated the effect of 5-hydroxydopa on survival in mice bearing i.p. or s.c. leukemia tumors and decreased survival relative to control mice bearing i.p. or s.c. pigmented and s.c. nonpigmented tumors. Ascorbate supplementation did not modify the effect of 5-hydroxydopa treatment on primary s.c. tumor growth in mice bearing melanoma or leukemia tumors nor did it affect ascites formation in treated mice bearing i.p. leukemia tumors. The lack of correlation between the observed inhibition of primary tumor growth and the absence of an effect on survival in 5-hydroxydopa-treated mice bearing i.p. melanoma may relate to an inability of this drug to interfere with tumor metastasis. These data argue against a role for 5-hydroxydopa as a metabolically derived cytotoxic formed in situ during concurrent treatment with levodopa Me ester [7101-51-1] and supplemental ascorbate.

IT 7101-51-1
RL: BIOL (Biological study)
(neoplasm inhibition mechanism of ascorbate and, neoplasm inhibition by ascorbate and hydroxydopa in relation to)
RN 7101-51-1 CAPLUS
CN L-Tyrosine, 3-hydroxy-, methyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L7 ANSWER 21 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN

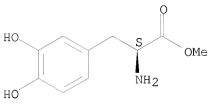
ACCESSION NUMBER: 1985:553567 CAPLUS
DOCUMENT NUMBER: 103:153567
ORIGINAL REFERENCE NO.: 103:24450h,24451a
TITLE: Modulation of peroxidation in murine melanoma by dietary tyrosine-phenylalanine restriction, levodopa methylester chemotherapy, and sodium ascorbate supplementation
AUTHOR(S): Pierson, Herbert F.; Meadows, Gary G.
CORPORATE SOURCE: Coll. Pharm., Washington State Univ., Pullman, WA, 99164-6510, USA
SOURCE: JNCI, Journal of the National Cancer Institute (1985), 75(3), 507-16
CODEN: JJIND8; ISSN: 0198-0157
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Treatment with the drug combination of levodopa methylester [7101-51-1] and benserazide [322-35-0], supplemental ascorbate [50-81-7], and dietary deficiencies of tyrosine [60-18-4] and phenylalanine [63-91-2] more than doubled the median survival time of female (C57BL/6 + DBA/2)F1 mice bearing B16 melanoma tumors. This study was designed to test the hypothesis that the antitumor activity of levodopa methylester and ascorbate against B16 melanoma is related to the generation of free radicals of O, which peroxidize lipid constituents of cell membranes leading to cell death. As an indication of lipid peroxidn., the individual and combined effects of drug treatment and ascorbate supplementation on host and tumor malondialdehyde levels were examined in mice fed one of three test diets (com., purified, or deficient) containing decreasing amts. of tyrosine and phenylalanine. Malondialdehyde levels were increased in the livers of all untreated tumor-bearing mice, which suggests that the tumor alters host antioxidant defenses. Drug treatment and ascorbate supplementation alone and in combination increased hepatic malondialdehyde levels inversely to the amts. of tyrosine and phenylalanine in the diet, and the effects of drug and ascorbate on malondialdehyde levels were additive. Plasma levels remained unchanged by drug treatment, ascorbate supplementation, or tumors in mice fed the com. or purified diets. Higher levels were observed only in tumor-bearing mice fed the deficient diet and given both drug treatment and ascorbate supplementation. Changes in tumor malondialdehyde levels generally correlated with the effects of the drug and ascorbate on survival time of mice bearing B16 melanoma. Tumors from mice fed the com. diet accumulated little malondialdehyde, and therapy was relatively ineffective in this dietary group. In mice fed purified or deficient diets, drug treatment and ascorbate supplementation alone increased survival and tumor malondialdehyde levels, but the level of peroxidn. in mice receiving the ascorbate supplementation was low compared to its greater antitumor effect on B16 melanoma. Although ascorbate enhanced the peroxidative activity of the drug on B16 melanoma tumors, the effects of the drug and ascorbate on malondialdehyde levels were not additive. Ascorbate enhanced survival of tumor-bearing mice that were fed the deficient diet and that were treated with drug, which indicated that ascorbate supplementation acted via other mechanisms. These results support the hypothesis that redox recycling occurs between ascorbate and o-dopaquinone, the active antitumor metabolite of levodopa, thus increasing lipid peroxidn. within B16 melanoma tumors, and that this peroxidative process is modulated by the levels of phenylalanine and tyrosine in the diet.

IT 7101-51-1
RL: BIOL (Biological study)
(peroxidn. in melanoma response to benserazide combination with, ascorbate and dietary deficiency of phenylalanine and tyrosine in relation to)

RN 7101-51-1 CAPLUS
CN L-Tyrosine, 3-hydroxy-, methyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



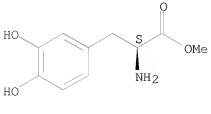
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L7 ANSWER 22 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1985:142798 CAPLUS
DOCUMENT NUMBER: 102:142798
ORIGINAL REFERENCE NO.: 102:22271a,22274a
TITLE: Inhibition of ribonucleotide reductase by antitumor agents related to levodopa and dopamine
AUTHOR(S): FitzGerald, George B.; Wick, Michael M.
CORPORATE SOURCE: Dana-Farber Cancer Inst., Harvard Med. Sch., Boston, MA, 02115, USA
SOURCE: Biochemical Pharmacology (1985), 34(3), 353-60 CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Using partially purified enzyme from L1210 cells, dihydroxybenzene derivs. related structurally to dopamine were shown to reversibly inactivate ribonucleotide reductase (I) [9040-57-7]. A structure-activity anal. revealed that derivs. with side-chains, which contain a neg. charged group, had significantly reduced inhibitory activity. The ability of these compds. to inhibit I was dependent on the OH groups being in the ortho position and did not correlate with free radical inhibitory activity. A kinetic anal. by the Lineweaver-Burk method indicated that I inhibition by 3,4-dihydroxybenzylamine [37491-68-2] was competitive with the reducing substrate dithioerythritol [6892-68-8]. This analog, in combination with hydroxyurea [127-07-1], gave synergistic inhibition of I, suggesting different sites of action. In Tween 80-treated, reversibly permeabilized L1210 cells, these drugs had an immediate inhibitory effect on I. Although these drugs had no immediate effect on DNA polymerase [9012-90-2], in permeabilized L1210 cells (when the cells were preincubated with the dihydroxybenzene derivs. for 1 h prior to permeabilization), there was significant inhibition of DNA polymerase activity. The 2 key enzymes for DNA synthesis appear to be sequentially inhibited by these analogs, with the reduced form (quinol) inhibiting I and the oxidized form (quinone) inhibiting DNA polymerase.

IT 7101-51-1
RL: BIOL (Biological study)
(DNA polymerase and ribonucleotide reductase of leukemia cells inhibition by)
RN 7101-51-1 CAPLUS
CN L-Tyrosine, 3-hydroxy-, methyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

L7 ANSWER 23 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1983:209676 CAPLUS
DOCUMENT NUMBER: 98:209676
ORIGINAL REFERENCE NO.: 98:31723a,31726a
TITLE: Sodium ascorbate enhancement of carbidopa-levodopa methyl ester antitumor activity against pigmented B16 melanoma
AUTHOR(S): Pierson, Herbert F.; Meadows, Gary G.
CORPORATE SOURCE: Coll. Pharm., Washington State Univ., Pullman, WA, 99164-6510, USA
SOURCE: Cancer Research (1983), 43(5), 2047-51
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

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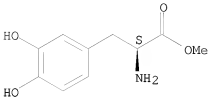
AB The single and combined antitumor activity on B16 melanoma in female C57BL/6 + DBA/2F1 mice bearing s.c. tumors of ascorbate (I) [50-81-7], carbidopa [28860-95-9]-levodopa Me ester [7101-51-1], and dietary phenylalanine [63-91-2] and tyrosine [60-18-4] deficiency is reported. Groups of mice were fed continuously 1 or 3 test diets both with and without Na ascorbate (30 mg/mL) in the drinking water beginning 2 wk before inoculation of 106 melanoma cells. The test diets included the following amts. of tyrosine-phenylalanine: com., 1.09 and 0.64%; purified, 0.6 and 0.3%; and deficient, 0.08 and 0.04%. Drug-treated groups received daily injections of carbidopa (100 mg/kg) and levodopa Me ester (1000 mg/kg) i.p. for 15 days beginning 1 day after tumor transplant. Tumor growth curves and median survival time were determined Ascorbate stimulated tumor growth in the com. diet group. In mice fed the purified diet, ascorbate inhibited growth in some tumors, while it had no effect on others. Ascorbate inhibited tumor growth in mice fed the deficient diet, which itself severely inhibited tumor growth, and in this group it increased survival by 82%. Drug treatment had little effect on tumor growth and survival of mice fed the com. diet, but it significantly decreased growth and moderately increased survival of mice fed the purified diet. The deficient diet enhanced drug activity and increased survival of tumor-bearing mice by 73%. Combined therapy had little effect in mice fed the com. diet; however, mice fed the purified diet and receiving drug and ascorbate had smaller tumors and lived 55% longer. In mice fed the deficient diet, the combination retarded tumor growth and increased survival by 123%. Adding ascorbate and restricting tyrosine and phenylalanine in combination with levodopa Me ester therapy may become an important strategy for treating malignant melanoma.

IT 7101-51-1
RL: BIOL (Biological study)
(melanoma therapy with ascorbate and carbidopa and, phenylalanine and tyrosine restriction in relation to)

RN 7101-51-1 CAPLUS
CN L-Tyrosine, 3-hydroxy-, methyl ester (CA INDEX NAME)

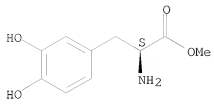
Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 12 THERE ARE 12 CAPLUS RECORDS THAT CITE THIS RECORD (12 CITINGS)

L7 ANSWER 24 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1982:490805 CAPLUS
DOCUMENT NUMBER: 97:90805
ORIGINAL REFERENCE NO.: 97:15141a,15144a
TITLE: Dietary influence of tyrosine and phenylalanine on the response of B16 melanoma to carbidopa-levodopa methyl ester chemotherapy
AUTHOR(S): Meadows, Gary G.; Pierson, Herbert F.; Abdallah, Rokia M.; Desai, Pankaj R.
CORPORATE SOURCE: Coll. Pharm., Washington State Univ., Pullman, WA, 99164, USA
SOURCE: Cancer Research (1982), 42(8), 3056-63
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The median survival of mice bearing slow-growing B16 melanoma averaged 8 days longer than that of mice bearing the fast-growing tumor. Median survival increased by 42% (slow-growing tumor) and by 30% (fast-growing tumor) in mice maintained on a chemical defined deficient diet (0.08% phenylalanine [63-91-2], 0.04% tyrosine [60-18-4]). Drug treatment (carbidopa [28860-95-9] 100, levodopa Me ester [7101-51-1] 1000 mg/kg, i.p. daily for 12 days) increased survival in mice maintained on purified (phenylalanine 0.6, tyrosine 0.3%) and deficient diets but was relatively ineffective in mice maintained on a com. diet (phenylalanine 1.09, tyrosine 0.64%) regardless of the tumor growth characteristics. Plasma tyrosine and phenylalanine levels decreased by 33 and 21%, resp., in mice maintained on the deficient diet and were unaffected by drug treatment. Tumors were 60% smaller in mice maintained on the deficient diet compared to mice maintained on the purified diet. Drug treatment resulted in decreased food intake and weight loss in all tumor-bearing dietary groups. Restricting food intake in untreated tumor-bearing mice to the amts. consumed by the drug treatment groups resulted in a parallel loss in body weight but no significant alteration in median survival. These data show that concomitant dietary tyrosine-phenylalanine restriction enhances the antitumor activity of carbidopa-levodopa Me ester against B16 melanoma.
IT 7101-51-1
RL: BIOL (Biological study)
(in melanoma chemotherapy, phenylalanine and tyrosine deficiency improvement of)
RN 7101-51-1 CAPLUS
CN L-Tyrosine, 3-hydroxy-, methyl ester (CA INDEX NAME)

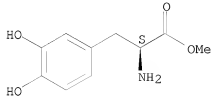
Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 15 THERE ARE 15 CAPLUS RECORDS THAT CITE THIS RECORD (15 CITINGS)

L7 ANSWER 25 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1982:118052 CAPLUS
DOCUMENT NUMBER: 96:118052
ORIGINAL REFERENCE NO.: 96:19323a,19326a
TITLE: Inhibition of reverse transcriptase by tyrosinase generated quinones related to levodopa and dopamine
AUTHOR(S): Wick, M. M.; Fitzgerald, G.
CORPORATE SOURCE: Sidney Farber Cancer Inst., Harvard Med. Sch., Boston, MA, 02115, USA
SOURCE: Chemico-Biological Interactions (1981), 38(1), 99-107
CODEN: CBINA8; ISSN: 0009-2797
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Several derivs. of levodopa have been shown to be potent inhibitors of the sulfhydryl enzyme, RNA-dependent DNA polymerase, reverse transcriptase (RT). In the presence of the polyphenol oxidase, tyrosinase, the inhibitory values were 10-6-10-5M. Structure-activity studies revealed that active oxidation or reduction was necessary for this potent inhibitory response. Spectrophotometric anal. showed that the presence of both the quinone and quinol was required for maximum inhibitory activity. These data suggest that the common intermediate of oxidation of quinols or reduction of quinones (i.e., semiquinone) is the active species. The use of tyrosinase provides a convenient model for the detection of the actual inhibitory interaction of a free-radical (semiquinone) with a biol. important macromol., RT.
IT 7101-51-1
RL: BIOL (Biological study)
(reverse transcriptase inhibition by)
RN 7101-51-1 CAPLUS
CN L-Tyrosine, 3-hydroxy-, methyl ester (CA INDEX NAME)

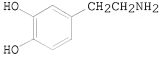
Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

L7 ANSWER 26 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1980:401160 CAPLUS
DOCUMENT NUMBER: 93:1160
ORIGINAL REFERENCE NO.: 93:231a,234a

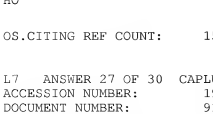
TITLE: Levodopa and dopamine analogs as DNA polymerase inhibitors and antitumor agents in human melanoma
AUTHOR(S): Wick, Michael M.
CORPORATE SOURCE: Sidney Farber Cancer Inst., Harvard Med. Sch., Boston, MA, 02115, USA
SOURCE: Cancer Research (1980), 40(5), 1414-18
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB The effects of levodopa [59-92-7], dopamine (I) [51-61-6], levodopa Me ester [7101-51-1], norepinephrine [51-41-2], and the analog 3,4-dihydroxybenzylamine [37491-68-2] on human and murine melanoma cells were examined When exponentially growing cells were exposed to these drugs, a characteristic inhibition of thymidine incorporation was observed with much less inhibition of either uridine or leucine incorporation. When melanoma cells were permeabilized by lysolecithin, thereby permitting the direct incorporation of labeled thymidine triphosphate, a similar inhibition of incorporation was observed I (4.8 μM) reduced the incorporation of the label by 50%. These results suggested that inhibition did occur at the level of DNA synthesis. In the presence of the melanocyte-specific oxidase, tyrosinase, these derivs. were potent inhibitors of isolated DNA polymerase [9012-90-2] α with 50% inhibitory concns. of 1-10 μM. The inhibition could be completely prevented by the presence of reducing agents such as dithiothreitol (1.0 mM). The quinols themselves were not inhibitors of DNA polymerase. Thus, I analogs represent an interesting class of antitumor agents with inhibitory activity for DNA polymerase.
IT 7101-51-1
RL: BIOL (Biological study)
(DNA polymerase-inhibiting and neoplasm-inhibiting activity of)
RN 7101-51-1 CAPLUS
CN L-Tyrosine, 3-hydroxy-, methyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 15 THERE ARE 15 CAPLUS RECORDS THAT CITE THIS RECORD (15 CITINGS)

L7 ANSWER 27 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1979:586573 CAPLUS
DOCUMENT NUMBER: 91:186573
ORIGINAL REFERENCE NO.: 91:29927a,29930a
TITLE: Levodopa and dopamine analogs: melanin

precursors as antitumor agents in experimental human and murine leukemia

AUTHOR(S): Wick, Michael M.

CORPORATE SOURCE: Sidney Farber Cancer Inst., Boston, MA, 02115, USA

SOURCE: Cancer Treatment Reports (1979), 63(6), 991-7
CODEN: CTRRDO; ISSN: 0361-5960

DOCUMENT TYPE: Journal

LANGUAGE: English

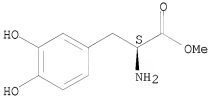
AB L-Dopa Me ester (I) [7101-51-1] has been shown to be a novel antitumor agent. Furthermore, the L-dopa analogs, D-dopa [5796-17-8] α-methyldopa [555-30-6], and dopamine [51-61-6], also exhibit significant antitumor activity in the L1210 and P388 lymphocytic leukemia systems. Structure-activity studies confirmed that the presence of a catechol moiety was essential for activity. Two analogs, 3,4-dihydroxybenzylamine [37491-68-2] and N-acetyldopamine [2494-12-4], which were much less neurotoxic, exhibited the greatest antitumor activity. In vitro, at concns. from 0.5 to 3.0 mM, there was a rapid inhibition of radiolabeled thymidine incorporation as compared to uridine or leucine incorporation. Continuous exposure of exponentially growing L1210 cells to I at similar concns. for up to 24 h resulted in a block of traverse of cells through the cell cycle in G1 coupled with a depletion of cells with a G2 complement of DNA. In vivo, toxicity of these compds. appears to be mediated principally by conversion to dopamine. Similar effects upon thymidine incorporation were observed in human leukemia cells in vitro.

IT 7101-51-1 71855-43-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(antileukemic activity of)

RN 7101-51-1 CAPLUS

CN L-Tyrosine, 3-hydroxy-, methyl ester (CA INDEX NAME)

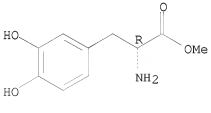
Absolute stereochemistry. Rotation (+).



RN 71855-43-1 CAPLUS

CN D-Tyrosine, 3-hydroxy-, methyl ester (CA INDEX NAME)

Absolute stereochemistry.



OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)

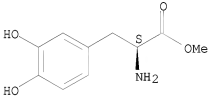
L7 ANSWER 28 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1978:101168 CAPLUS

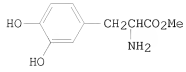
DOCUMENT NUMBER: 88:101168

ORIGINAL REFERENCE NO.: 88:15825a,15828a
TITLE: A simple procedure for distinguishing dopamine from noradrenaline in peripheral nervous structures in the fluorescence microscope
AUTHOR(S): Hess, Arthur
CORPORATE SOURCE: Rutgers Med. Sch., Coll. Med. Dent. New Jersey, Piscataway, NJ, USA
SOURCE: Journal of Histochemistry and Cytochemistry (1978), 26(2), 141-4
CODEN: JHCYAS; ISSN: 0022-1554
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The difference between dopamine and noradrenaline after ordinary histofluorescent procedures cannot be discerned. Reserpine treatment results in depletion of fluorescent material from dopaminergic and noradrenergic peripheral nervous structures. Administration of reserpine, 1 mg/kg s.c. for 3 h, followed by i.p. injection of 200 mg/kg levodopa Me ester in 0.9% saline for 90 min, result in refluorescence of dopaminergic (glomus cells of the carotid body) but not noradrenergic (sympathetic ganglion cells, nerves of atrial heart muscle and blood vessels) structures. Hence, the sequential administration of these readily available drugs and the application of ordinary histofluorescent techniques result in a simple procedure for distinguishing dopamine from noradrenaline in the fluorescence microscope.
IT 7101-51-1
RL: ANST (Analytical study)
(dopamine and noradrenaline differentiation in peripheral nervous system in response to reserpine and)
RN 7101-51-1 CAPLUS
CN L-Tyrosine, 3-hydroxy-, methyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



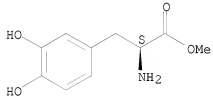
L7 ANSWER 29 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1977:561696 CAPLUS
DOCUMENT NUMBER: 87:161696
ORIGINAL REFERENCE NO.: 87:25491a,25494a
TITLE: Ethanol, levodopa and inhibitors of extracerebral aromatic L-amino acid decarboxylase: a drug-drug interaction study
AUTHOR(S): Messiha, F. S.
CORPORATE SOURCE: Dep. Pharmacol., Texas Tech Univ. Sch. Med., Lubbock, TX, USA
SOURCE: Proceedings of the Western Pharmacology Society (1977), 20, 327-31
CODEN: PWPSA8; ISSN: 0083-8969
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

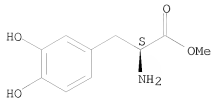
AB L-dopa Me ester (I) [7101-51-1] (500 mg/kg, i.p.) given to rats during the period of EtOH intake resulted in the death of about 55% of the rats, but the toxic effects could be nullified by pretreatment with an extracerebrally acting dopa decarboxylase [9042-64-2] inhibitor, benserazide [322-35-0]. Carbidopa [28860-95-9] (50 mg/kg) administered to rats decreased EtOH intake, but 200 mg carbidopa/kg was toxic.
IT 7101-51-1
RL: BIOL (Biological study)
(toxicity of ethanol and, benserazide effect on)
RN 7101-51-1 CAPLUS
CN L-Tyrosine, 3-hydroxy-, methyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L7 ANSWER 30 OF 30 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1977:527202 CAPLUS
DOCUMENT NUMBER: 87:127202
ORIGINAL REFERENCE NO.: 87:20125a,20128a
TITLE: Possible mechanism of adverse reaction following levodopa plus benserazide treatment
AUTHOR(S): Messiha, F. S.
CORPORATE SOURCE: Sch. Med., Texas Tech. Univ., Lubbock, TX, USA
SOURCE: British Journal of Pharmacology (1977), 60(1), 55-7
CODEN: BJPCBM; ISSN: 0007-1188
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Administration of benserazide [322-35-0] (500 mg/kg, i.p., daily for 7 days) alone or in combination with L-DOPA Me ester [7101-51-1] (500 mg/kg, i.p., daily for 7 days) to rats, decreased liver aldehyde dehydrogenase (EC 1.2.1.3) [9028-86-8] activity without affecting that of alc. dehydrogenase (EC 1.1.1.1) [9031-72-5]. Administration of L-DOPA alone for 7 days did not affect either enzyme activity. The combined treatment might be conducive to the in vivo formation of L-DOPA-derived tetrahydroisoquinoline derivs. which might be implicated in L-DOPA-produced adverse effects.
IT 7101-51-1
RL: BIOL (Biological study)
(alc. dehydrogenase and aldehyde dehydrogenase of liver response to, benserazide interaction with)
RN 7101-51-1 CAPLUS
CN L-Tyrosine, 3-hydroxy-, methyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).


HO
HO
S
O
OMe
NH2